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L2	cationic lipid	8938	L2
L1	conjugated lipid or liposome	61789	L1

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L28: Entry 12 of 29 File: PGPB Jun 13, 2002

PGPUB-DOCUMENT-NUMBER: 20020072121
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020072121 A1

TITLE: Methods of enhancing SPLP-mediated transfection using endosomal membrane destabilizers

PUBLICATION-DATE: June 13, 2002

US-CL-CURRENT: 435/458; 435/320.1, 536/23.2

APPL-NO: 09/ 839707 [PALM]
DATE FILED: April 20, 2001

RELATED-US-APPL-DATA:
Application 09/839707 is a continuation-in-part-of US application 09/553639, filed April 20, 2000, PENDING
Application is a non-provisional-of-provisional application 60/227949, filed August 25, 2000,

CROSS-REFERENCES TO RELATED APPLICATIONS

[0001] This patent application claims the benefit of U.S. Provisional Patent Application No. 60/227,949, which was filed Aug. 25, 2000, U.S. patent application Ser. No. 09/553,639, which was filed Apr. 20, 2000, and PCT Patent Application No. CA 00/00451, which was filed Apr. 20, 2000, the teachings of both of which are incorporated herein by reference.

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
CA	00/00451	2000CA-00/00451	April 20, 2000

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L28: Entry 21 of 29 File: USPT Nov 5, 2002

DOCUMENT-IDENTIFIER: US 6475757 B2
TITLE: Plasmids for construction of eukaryotic viral vectors

Detailed Description Text (42):
pDesired-.phi. packaged in wild type or modified phage capsids can be used to deliver transgenes to target cells. The packaged pDesired-.phi. is contacted to a eukaryotic cell. The eukaryotic cell internalizes the encapsidated pDesired-.phi.. Through this internalization process, the encapsidated DNA becomes substantially free of the capsid proteins that surround it, so that each gene of the pDesired-.phi. that is capable of being expressed in the target eukaryotic cell can be transcribed and translated and the viral vector can replicate. Preferably, the targeted pDesired-.phi. phage is internalized with an endosomolytic agent so that the endosomolytic agent ruptures the endosomes containing the agent and the pDesired-.phi.. It is known that such rupture significantly increases the efficiency of expression of the gene transfer vector. Examples of endosomolytic agents useful in the context of the present invention include chloroquine, calcium phosphate particles, adenoviral coat proteins (including adenoviral virions), and adeno-associated viral coat proteins (including AAV virions).

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L28: Entry 26 of 29 File: USPT Aug 7, 2001

DOCUMENT-IDENTIFIER: US 6270761 B1
TITLE: Delivery of nucleic acid

Brief Summary Text (9):
Molecular conjugate vectors were developed to overcome some of the limitations of previous nonviral gene delivery systems. The major limitation with calcium phosphate transfection was the inefficiency with which DNA delivered as a calcium phosphate co-precipitate could escape from endosomal vesicles into the cytosol. In molecular conjugate vectors, receptor-mediated endocytosis of the DNA is achieved by complexing it to a macromolecular ligand and escape from the endosome is achieved by adding an endosomolytic agent to the complex, such as an adenovirus particle (Michael & Curiel, 1994 Gene Therapy I p223-232)..

Brief Summary Text (13):
In a second aspect the invention provides a composition for delivering a nucleic acid to a target cell, comprising the nucleic acid to be delivered, an endosomolytic moiety, and a calcium salt in particulate form. Preferably the calcium salt is complexed with the other components of the composition.

Brief Summary Text (21):
One limitation of calcium phosphate crystals is that they do not provide, per se, any mechanism for the endocytosed DNA or RNA to escape from the endosomes. Therefore, based on the inventors' novel observation that they also have a high affinity for endosomolytic adenovirus particles, it is preferred to prepare calcium phosphate/nucleic acid/endosomolytic moiety complexes in which the endosomolytic moiety (typically an adenovirus) will facilitate endosomal escape of the nucleic acid. This will greatly enhance the efficiency with which the nucleic acid is translocated to the cell nucleus. As an alternative to the use of adenovirus, it should also be possible to incorporate purified endosomolytic proteins into calcium phosphate-nucleic acid complexes, since calcium phosphate also has a high affinity for proteins. Many endosomolytic proteins are known (see for example Plank et al., 1994 J. Biol. Chem. 269, 12,918-12,924).

Brief Summary Text (32):
Also, in light of the observation that the endosomolytic properties of adenovirus particles can be employed to facilitate gene transfer by retroviral vectors to cells outside of their normal host range (Adams et al 1995 J. Virol. 69 p-1894), it is proposed to prepare calcium phosphate-retrovirus-adenovirus complexes (e.g. co-precipitates) in which the calcium phosphate will facilitate contact with the target cells and carriage of the viruses into the endosomal compartment, and the adenovirus moiety will facilitate endosomal escape of the endocytosed retrovirus.

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L28: Entry 27 of 29 File: USPT Jun 3, 1997

DOCUMENT-IDENTIFIER: US 5635380 A
TITLE: Enhancement of nucleic acid transfer by coupling virus to nucleic acid via lipids

Brief Summary Text (22):
The present invention provides a method of enhancing the delivery of a nucleic acid, into a cell, comprising forming a complex comprising the nucleic acid, a cationic liposome and a virus and administering the complex to the cell, thereby enhancing the delivery of the nucleic acid into the cell. Delivery to a cell includes the nucleic acid being internalized to some area within the cell membrane, e.g., into a vesicle, the cytoplasm, an endosome, the nucleus, etc. By "enhancing" is included that a higher efficiency of delivery of a nucleic acid into a cell, which cell can be in a subject, can be obtained than with the nucleic acid alone (such as with standard methods as electroporation, calcium phosphate precipitation, etc.), the nucleic acid with liposomes alone, or the nucleic acid with virus alone. Additionally, the present method enhances gene delivery at a higher efficiency of transfer than previously known methods. The enhancement of gene transfer can occur by, for example, enhanced entry of the nucleic acid into the cell, mediated by both virus and liposomes, and due to virus causing lysis of the endosome, thereby preventing degradation of the nucleic acid (complexed with the virus) in the endosome.

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